

Amendments to the Specification:

1. Please replace the last paragraph at page 1, from line 23 on page 1 through line 11 on page 2, with the following paragraph:

-- ~~TAQMANTa~~~~Man~~ was the first homogenous assay capable of detecting single nucleotide polymorphisms (U.S. Patents 5,723,591). In this assay, two PCR primers flank a central probe oligonucleotide. The probe oligonucleotide comprises two fluorescent moieties. During the polymerization step of the PCR process, the polymerase cleaves the probe oligonucleotide. The cleavage causes the two fluorescent moieties to become physically separated, which causes a change in the wavelength of the fluorescent emission. As more PCR product is created, the intensity of the novel wavelength increases. While TaqMan accomplishes the goal of single nucleotide detection in a homogenous assay, it has two disadvantages. The first is that each nucleotide to be detected requires a different oligonucleotide probe comprising two different fluorescent moieties. Such probes must be custom-synthesized and are thus expensive. The second disadvantage is that TaqMan probes are not very discriminating for single nucleotide differences. Thus there can be significant false-positive signals.--

2. Please replace the first full paragraph at page 2, lines 12-21, with the following paragraph:

-- Molecular Beacons are an alternative to ~~TAQMANTa~~~~Man~~ (U.S. Patent Nos. 6,277,607; 6,150,097; 6,037,130). Molecular Beacons undergo a conformational change upon binding to a perfectly matched template. The conformational change of the Beacon increases the physical distance between a fluorophore moiety and a quencher moiety on the Beacon. This increase in physical distance causes the effect of the quencher to be diminished, thus increasing the signal derived from the fluorophore. Molecular Beacons are more discriminating of single nucleotide differences, as compared with TaqMan probes. However they still require the synthesis of a custom oligonucleotide (the Beacon) having two different fluorescent moieties for each target sequence being examined. Thus the technology is expensive.—

3. Please replace the second full paragraph at page 2, lines 22-25, with the following paragraph:

-- There are several other fluorescent and enzymatic PCR technologies, such as SCORPIONS~~Scorpions~~<sup>TM</sup>, SUNRISE~~Sunrise~~<sup>TM</sup> primers, and DNAzymes. Not all of these are suitable for single nucleotide detection, and most of them require the synthesis of a custom, fluorescently labeled oligonucleotide for each target nucleotide.—

4. Please replace the second full paragraph at page 20, lines 15-16, with the following paragraph:

-- As used herein, the term “T<sub>m</sub>” is used in reference to the “melting temperature”. The melting temperature is the temperature at which 50% of a population of double-stranded polynucleotide molecules becomes dissociated into single strands. The equation for calculating the T<sub>m</sub> of polynucleotides is well-known in the art. The T<sub>m</sub> of a hybrid polynucleotide is often estimated using a formula adopted from hybridization assays in 1 M salt, and commonly used for calculating T<sub>m</sub> for PCR primers: {(number of A+T) x 2°C + (number of G+C) x 4°C}, see, for example, C. R. Newton et al. PCR, 2nd Ed., Springer-Verlag (New York: 1997), p. 24. This formula was found to be inaccurate for primers longer than 20 nucleotides. Other more sophisticated computations exist in the art which take structural as well as sequence characteristics into account for the calculation of T<sub>m</sub>. A calculated T<sub>m</sub> is merely an estimate; the optimum temperature is commonly determined empirically.—

5. Please replace the fourth full paragraph at page 36, lines 12-19, with the following paragraph:

-- Other useful fluorophores (in addition to those listed in Tables 1-4) include, but are not limited to: TEXAS RED~~Texas Red~~<sup>TM</sup> (TR~~Sulforhodamine 101- $\alpha$ -bungarotoxin~~), LISSAMINE~~Lissamine~~<sup>TM</sup> rhodamine B (1, 2-dihexadecanoyl-sn-glycero-3-phosphoethanolamine), OREGON GREEN~~Oregon Green~~<sup>TM</sup> 488 (2',7' - difluorofluorescein), carboxyrhodol and carboxyrhodamine, OREGON GREEN~~Oregon Green~~<sup>TM</sup> 500 (C<sub>20</sub>H<sub>10</sub>F<sub>2</sub>O<sub>8</sub>S), 6 - JOE (6 - carboxy - 4',5' - dichloro - 2',7' - dimethoxyfluorescein, eosin F3S (6 -

carboxymethylthio - 2',4', 5',7' - tetrabromo - trifluorofluorescein), CASCADE BLUE easeade blue™ (Cbethylenediamine trisodium), aminomethylcoumarin (AMC), pyrenes, dansyl chloride (5 - dimethylaminonaphthalene - 1 - sulfonyl chloride) and other naphthalenes, PyMPO, ITC (1 - (3 - isothiocyanatophenyl) - 4 - (5 - (4 - methoxyphenyl)oxazol - 2 - yl)pyridinium bromide).—

6. Please replace the second full paragraph at page 38, lines 8-25, with the following paragraph:

-- The donor and acceptor groups may independently be selected from suitable fluorescent groups, chromophores and quenching groups. Donors and acceptors useful according to the invention include but are not limited to: 5 - FAM (also called 5 - carboxyfluorescein; also called Spiro(isobenzofuran - 1(3H), 9' - (9H)xanthene) - 5 - carboxylic acid, 3',6' - dihydroxy - 3 - oxo - 6 - carboxyfluorescein); 5 - Hexachloro - Fluorescein ([4,7,2',4',5',7' - hexachloro - (3',6' - dipivaloyl - fluoresceinyl) - 6 - carboxylic acid }); 6 - Hexachloro - Fluorescein ([4,7,2',4',5',7' - hexachloro - (3',6' - dipivaloylfluoresceinyl) - 5 - carboxylic acid }); 5 - Tetrachloro - Fluorescein ([4,7,2',7' - tetra - chloro - (3',6' - dipivaloylfluoresceinyl) - 5 - carboxylic acid}); 6 - Tetrachloro - Fluorescein ([4,7,2',7' - tetrachloro - (3',6' - dipivaloylfluoresceinyl) - 6 - carboxylic acid}); 5 - TAMRA (5 - carboxytetramethylrhodamine; Xanthylium, 9 - (2,4 - dicarboxyphenyl) - 3,6 - bis(dimethyl - amino); 6 - TAMRA (6 - carboxytetramethylrhodamine; Xanthylium, 9 - (2,5 - dicarboxyphenyl) - 3,6 - bis(dimethylamino); EDANS (5 - ((2 - aminoethyl) amino)naphthalene - 1 - sulfonic acid); 1,5 - IAEDANS (5 - (((2 - iodoacetyl)amino)ethyl) amino)naphthalene - 1 - sulfonic acid); DABCYL (4 - ((4 - (dimethylamino)phenyl) azo)benzoic acid) Cy5 (Indodicarbocyanine - 5) Cy3 (Indo - dicarbocyanine - 3); and BODIPY FL (2,6 - dibromo - 4,4 - difluoro - 5,7 - dimethyl - 4 - bora - 3a,4a - diaza - s - indacene - 3 - propionic acid), Rox, as well as suitable derivatives thereof.—